REMARKS

Claims 1, 3, 6, 8-28, and 123 are pending. Claim 3 was amended to correctly match the antecedent. A new claim 123 was added. Support for claim 123 can be found in the previous claim 3 and throughout the specification, for example, at page 5, lines 11-30. Applicants submit that the amendment and the new claim do not introduce new matter and it does not change the scope of the claim.

Rejections under 35 U.S.C. §103(a)

Claims 1, 3, 12-15, 20, and 23-28 were rejected under 35 U.S.C. §103(a) as unpatentable over WO 93/04692 (the "'692 publication") in view of the U.S. Patent No. 6,096,706 ("Toback").

The Examiner asserts that the '692 publication discloses regeneration of damaged tissue and that it provides examples for such regeneration after the onset of injury. Applicants respectfully submit that the '692 publication in view of Toback does not teach or suggest the claimed invention for the reasons below.

Claims 1 and 3, and all claims dependent therefrom, recite "creating a local defect site." This local defect site is used to evaluate a candidate morphogen. As explained in the specification at page 11, lines 15 to 16, "defect site" means "any structural disruption in a tissue or organ requiring a repair." According to the Webster's Revised Unabridged Dictionary (1998), "disrupt" means to break asunder, or to rend. The specification of the present invention describes how such disruption can be created by implanting a matrix material or by creating a fracture or a tear. The specification fully describes, with examples, what a local defect site is and how to create them. (See, for example, page 9, line 21 to page 10, line 8, and the section IV, entitled Bioassay starting from page 39, line 12.) A candidate morphogen is then administered systemically, and the repair of these local defect sites is examined to evaluate the morphogen.

In contrast, the '692 publication does not teach or suggest creating a local defect site to evaluate a morphogen candidate by systemic administration. In particular, the examples in the '692 publication cited by the Examiner to support her contention that the '692 publication teaches treatment with morphogen after the onset of injury, involve ischemia-reperfusion injury

or injection of collagen material to induce inflammation in the target tissue, neither example involving creating a local defect site as defined in the specification. The ischemia-reperfusion injury described in Examples 3 and 6 generally affects the organ or tissue that is supplied by the occluded blood vessel. The injury caused by such ischemia-reperfusion can be distinguished from creating local defect site taught by the instant specification because it is not a "structural disruption," and because it is a consequence of ischemia-reperfusion, not a directly created "local defect." The extent and degree of such consequential damage is not as well defined as the well-defined local defect site created in the instant application. Example 14 pertains to systemic inflammation and damages induced by collagen injection. Systemic inflammation is not a local defect. Therefore, the '692 publication does not teach or suggest creating a local defect site that is used to evaluate a systemically administered candidate morphogen.

Combining Toback does not make the present invention obvious to one skilled in the art. Toback describes novel polypeptides derived from Wound Growth Factor, which promote the growth of kidney epithelial cells *in vitro* and which is useful in kidney repair after acute renal failure induced by injecting mercuric chloride. Nothing in Toback teach or suggest creating a local defect site, which is structural disruption of a tissue or organ, or repairing an already-created local defect site.

Claims 3, 6, and 8-28 were also rejected under 35 U.S.C. §103(a) as unpatentable over WO 93/04692 in view of Toback and Benet et al. As described above, Applicants submit that the '692 publication in view of Toback does not teach or suggest the claimed invention. Further considering Benet does not provide what is lacking from the '692 publication and Toback. Benet describes dosage optimization, but does not provide any information regarding creating a local defect site to evaluate a morphogen candidate, or to repair an already-created local defect site.

In view of the above comments, Applicants believe that pending application is in condition for allowance, and respectfully request that the Examiner withdraw the rejections.

Applicant believes no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. JJJ-P01-570 from which the undersigned is authorized to draw.

Dated: November 17, 2004.

Respectfully submitted,

By _____

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